Hepatoblastoma and Wilms' Tumour in an Infant with Beckwith-Wiedemann Syndrome and Diazoxide Resistant Congenital Hyperinsulinism

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Introduction

- Beckwith-Wiedemann Syndrome (BWS) could be associated with embryonal tumours and congenital hyperinsulinism (CHI)
- We report a case of BWS secondary to paternal uniparental disomy of chromosome 11 [UPD(11)pat] with diazoxide resistant congenital hyperinsulinism (CHI), and early onset atypical hepatoblastoma and Wilms' Tumour

Case description

- The infant presented with recurrent hypoglycaemia requiring high intravenous glucose infusion and was biochemically confirmed to have CHI. He was resistant to diazoxide but responded well to octreotide and was switched to lanreotide at 1 year of age.
- Genetic analysis for ABCC8 and KCNJ11 were negative. He had clinical features suggestive of BWS. Genetics revealed hypomethylation at KCNQ1OT1:TSS-DMR and hypermethylation at H19/IGF2:IG-DMR consistent with mosaic UPD(11p15). Hepatoblastoma was detected on day 4 of life. It was resistant to chemotherapy, hence it was surgically resected.
- He developed Wilms' tumour at 3 months of age which showed a poor response to induction chemotherapy with vincristine and actinomycin D; hence post-operative chemotherapy had to be intensified with cycles containing cyclophosphamide, doxorubicin, carboplatin and etoposide, in addition to receiving flank radiotherapy.

Table 1. Trend in Alfa Fetoprotein (AFP) levels in the first year of life

Age (days)	AFP (iu/mL)	AFP Normal Range* (iu/mL)	Comment
4	128,729	4,396 – 91,008	At diagnosis of hepatoblastoma
73	13,207	5 – 867	Pre-operative (hepatoblastoma resection)
118	1713	2.5 – 346	Post-operative (hepatoblastoma resection)
177	213	1 – 107	Follow up at 6 months
378	15	0.7 – 72	Follow up at 1 year

Figure 1 Macroglossia

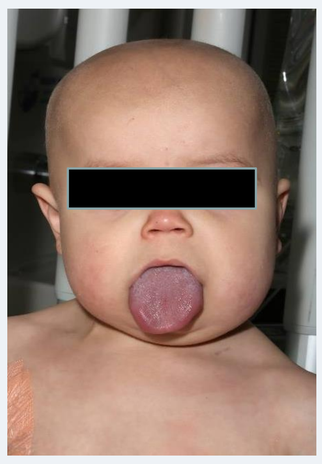


Figure 2 Relatively well differentiated hepatoid cells arranged in chords and tabaculae

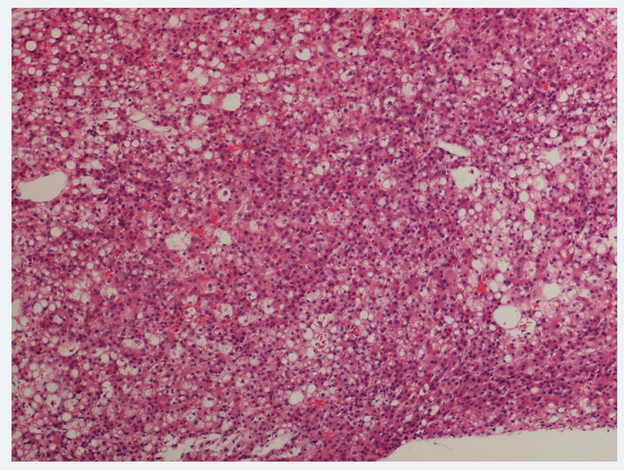


Figure 3 Blastemal element of Wilms tumour seen as nodule of undifferentiated round blue cells

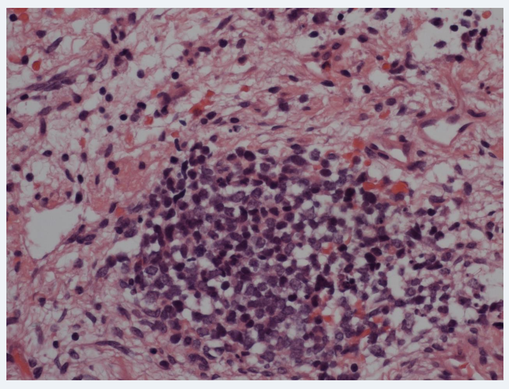
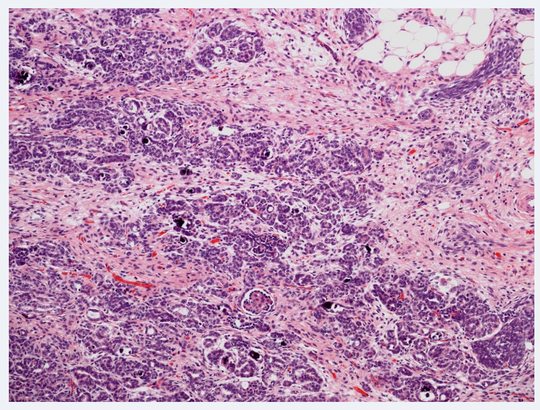


Figure 4 Epithelial elements of Wilms' tumour seen as tubules and glomeruloid bodies



Established Facts

- Beckwith-Wiedemann Syndrome is a genetic disorder with multiple molecular mechanisms and variable phenotypes
- Hyperinsulinism in BWS may show variable response to diazoxide
- Embryonal tumours are common in BWS during early childhood years

Novel Insights

- Long acting somatostatin analogues are effective in managing persistent CHI in BWS
- UPD (11) pat genotype may be a pointer to persistent and severe CHI
- Tumours with earlier onset may be resistant to recognized first line chemotherapy
- The early appearance and rapid progression of Hepatoblastoma and Wilms' tumour in this case might necessitate a more frequent screening protocol with frequent abdominal ultrasound in UPD(11)pat genotype patients than the currently recommended 3 monthly schedule

The authors have nothing to disclose